



neuroendocrine and circadian systems that influence mood, behaviour and cognition. The interaction between these systems is multifactorial and complex, and it is unlikely that a simple etiologic factor explains the symptoms of PDD. From a treatment point of view all trials to date have demonstrated a strong placebo effect. Benefits of nutritional approaches are unsure. Doses of vitamin B6 up to 100mg daily are likely to give some benefit. There is limited evidence to support the role of only group therapy, lifestyle modification, cognitive therapy and physical intervention such as relaxation although when in combination with pharmacologic therapy, they do have benefits. Progestogens given during the luteal phase of the menstrual cycle are not effective. Suppression of ovulation with the OCP may or may not be of benefit. Suppression of ovulation with transdermal estradiol, combined with progestogen for endometrial protection, is effective in approximately 50% of women. Danazol is effective, but is not suitable for long term use. GnRH analogues are effective for severe PMS with add-back therapy in the form of tibolone. Oophorectomy should only be considered in severe PMS when medical measures have failed, and only if preceded by a trial of GnRH agonist therapy. Aldactone and bromocryptine have a role. Tri-cyclic antidepressants and benzodiazepenes are not effective. The presence of high baseline symptom scores (premenstrual magnification) is an important contributor to treatment failure. SSRI's are most effective in the management of PMS and PMDD.

First line treatment, mainly the result of ease of administration and tolerability, is now considered serotonergic antidepressants. Four double-blind studies with fluoxetine, 20mg/day, resulted in impressive efficacy and relative lack of side-effects. Two open long-term studies have indicated the efficacy of fluoxetine over an extended period of time. In fact there are a number of studies to substantiate that all SSRI's and SSNRI's are most effective in managing women with PMS and PDD symptomatology. Administration of the medication can be daily and throughout the cycle, or in the form of partial-cycle (luteal) administration only or taking lower doses during the follicular phase with an increase in dose during the luteal phase. Luteal administration of alprazolam or buspirone is also a reasonable choice. If the use of psychotropic medications is not successful, GnRH analogs with add-back regimen should then be tried.

The Menopause

More controversial than the physical symptoms of

menopause is the question of the existence of a menopause related affective disorder. Studies of menopause and depression have been problematic because of variable definitions of menopause and depression. Although the evidence for increased rates of major depression at menopause is lacking there may be a psychological syndrome of symptoms of more minor severity during the pre-menopausal years. Such a menopausal related mood syndrome includes symptoms of depression, anxiety, irritability, fatigue, insomnia, forgetfulness, decreased self esteem and decreased libido. Some studies seem to confirm that if psychological symptoms are present, they are more likely to occur before the cessation of menses, rather than after.

The relationship between affective disorder and PDD is more robust than

that between affective disorder and menopause. Women with PDD not only have elevated rates of prior major depression but are also more likely to present with affective disorders during the menopause. Menopause is not a time of increased expression of major depression based on community surveys. However, women who have major depression at the time of menopause are likely to have had prior depressive episodes, postpartum affective syndromes or PDD. Menopause seems to be a time of increased risk for expression of affective disorders in these women.

The widespread use of HRT has raised the question of psychological side-effects of ovarian steroid hormones. Some minor symptoms may respond to HRT. Estrogen modulates serotonin and increases tritiated imipramine platelet binding in women, which in turn increases serotonin presynaptic re-uptake. Tritiated imipramine binding is reduced in depression, and this is a possible mechanism by which estrogen may improve mood. Estrogen modulates norepinephrine levels, decreases monoamine oxidase levels, affects dopamine turnover and endorphin levels, increases brain excitability, and possibly interacts with gamma-aminobutyric acid (GABA).

Estrogen improves mood and increases the sense of wellbeing in menopausal women. It appears that in non-depressed or mildly depressed women, estrogen replacement may be helpful in elevating mood and improving their sense of wellbeing. In women who are clinically depressed, it is unclear whether estrogens alone can elevate mood to a clinically significant degree. For depressed women who take antidepressants, estrogen's use as an adjunct is unclear at this stage. There is some data to support that progestogens may promote depression. Combined versus sequential HRT, and natural versus synthetic progesterone preparations may have different effects on promoting dysphoria. Dose and preparation of progesterone are important.

Recent data seems to support that estrogen replacement in the menopausal women having panic disorders may be of some value. Symptoms that are associated with panic disorders include palpitations, sweating, trembling or shaking, sensations of shortness of breath, feeling of choking, chest pain or discomfort, nausea, feeling dizzy or light headed, de-realisation, de-personalisation, fear of losing control or going crazy, fear of dying, parasthesia, chills and/or hot flushes.

Depression and Somatisation Disorder

Not only is there a relationship between reproductive